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ORIGINAL ARTICLES

# Adaptive Closed-Loop Control Provides Blood-Glucose Regulation Using Dual Subcutaneous Insulin and Glucagon Infusion in Diabetic Swine

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## Abstract

***Background:***

In order to stave off deleterious complications of the disease, the ultimate task for people with diabetes is to maintain their blood glucose in euglycemic range. Despite technological advancements, conventional open-loop therapy often results in prolonged hyperglycemia and episodic hypoglycemia, in addition to necessitating carbohydrate counting, frequent glucose monitoring, and drug administration. The logical conclusion in the evolution of exogenous insulin therapy is to develop an automated closed-loop control system.

***Methods:***

Eleven closed-loop control experiments were conducted in four anesthetized diabetic pigs, with carbohydrate loads simulated by intravenous glucose administration through ear-vein catheters. Type 1 diabetes-like pathology was induced using intravenous administration of cytotoxin streptozotocin. The augmented model-predictive control algorithm accounts for the accumulation of subcutaneous insulin, which is critical in avoiding excessive insulin dosing.

***Results:***

Control results consistently showed successful blood-glucose regulation to euglycemic range within 80–120 minutes after intravenous glucose loads, with no incidence of hypoglycemia. This is consistent with a negative oral glucose tolerance test for diabetes and is the optimal postprandial regulation that can be achieved with subcutaneous insulin administration. Results also demonstrated the potency of subcutaneous glucagon in staving off episodic hypoglycemia and revealed efficacy of the control algorithm in coping with a twofold variation in subject weights, while simultaneously overlooking erratic blood-glucose fluctuations.

***Conclusions:***

Using an automated adaptive glucose-control system, we show successful blood-glucose regulation *in vivo* and establish, definitively, the plausibility and practicality of closed-loop blood-glucose control using subcutaneous insulin and glucagon infusion in type 1 diabetes. The control system strikes an intricate balance between tight blood-glucose control and optimal drug consumption, while simultaneously maintaining emphasis on simplicity and reliability.

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**Abbreviations:** (BG) blood glucose, (GPC) generalized predictive control, (IV) intravenous, (STZ) streptozotocin, (SC) subcutaneous

**Keywords:** counterregulatory hormone, hyperglycemia, hypoglycemia, infusion pump, *in vivo*, predictive control, swine

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